

Applicant : Willner et al.
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REMARKS

Claims 9 to 22 and 34 to 47 have been cancelled. Applicants have amended the claims 1, 3, 23 and 28 to address objections made by the examiner. Applicants appreciate the notification that claims 32 and 33 would be allowable if rewritten in independent form.

The references listed on pages 1 and 2 of the specification were listed in Information Disclosure Statements filed March 11, 2003 and July 21, 2003.

Rejections Under 35 U.S.C. §112, first paragraph (written description)

The examiner rejected claims 1-9 as failing to meet the written description requirement because, according to the examiner, the specification does not support the limitation "by measuring insulation of the sensing interface to interfacial electron transfer between the sending interface and the surrounding medium".

The specification provides written description support for the limitation "by measuring insulation of the sensing interface to interfacial electron transfer between the sensing interface and the surrounding medium", for example, page 5, lines 23-25 and page 14, lines 3-12. The specification clearly explains that the presence of the verification oligonucleotide on the sensing interface can be detected by measuring the insulation of the sensing surface to electron transfer between the sensing interface and the surround medium. In view of this disclosure, Applicants respectfully request that the rejections under 35 U.S.C. §112, first paragraph be withdrawn.

Rejections Under 35 U.S.C. §112, second paragraph (written description)

The Examiner rejected claim 26 as allegedly indefinite for reciting a "microbalance quartz-crystal probe". Applicants have amended claim 26 to recite a "quartz crystal microbalance" Such devices are well-known in the art, see, e.g., page 6, lines 1-5 of the specification, and Applicants submit that claim 26 is clear and definite.

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Rejections Under 35 U.S.C. §102(e)

Blackburn et al.

The examiner rejected claims 1 and 2 as anticipated by Blackburn et al. (U.S. Patent No. 6,686,150; "Blackburn").

The methods of claims 1 and 2 entail detecting the presence of a particular oligonucleotide on a sensing interface "by measuring insulation of the sensing interface to interfacial electron transfer between the sensing interface and the surrounding medium". Thus, the presence of a particular oligonucleotide, here the "verification oligonucleotide" is detected because the presence of the oligonucleotide leads to insulation of the sensing surface from electron transfer between the surface and the surrounding medium. This insulation can arise, for example, because the oligonucleotide is bound to a moiety that converts a substrate to a product that is deposited on the sensing surface, leading to insulation of the sensing surface. In any event, it is the insulation of the sensing surface to electron transfer from the surrounding medium that is used to detect the presence of the oligonucleotide.

Blackburn describes a very different approach to detecting the presence of an oligonucleotide. The methods of Blackburn employ an oligonucleotide that is linked to a electron transfer moiety (ETM) such as ferrocene. The oligonucleotide is detected by measuring electron transfer between the ETM and the electrode - not between the surrounding medium and the electrode as suggested by the examiner. The examiner refers to column 92 of Blackburn and argues that "insulators (such as resistance) is used to monitor electron transfer between RTM and the electrode ... and the measurement .. must be performed in or through the hybridization buffer." The examiner's argument is misplaced. No matter what method is used to measure electron transfer in Blackburn, it is electron transfer between the ETM and the electrode that is measured, NOT electron transfer between the electrode and the surrounding medium. Because of this fundamental difference, Blackburn cannot anticipate the presently claimed invention.

In view of the forgoing, applicants respectfully request that the rejections under 35 U.S.C. §102(e) based on Blackburn be withdrawn.

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Durst et al.

The examiner rejected claims 23-26, 28, 29 and 31 as anticipated by Durst et al. (U.S. Patent No. 6,358,752; "Durst").

The examiner argues that Durst discloses a device which meets the limitations of the current claims because a capturing oligonucleotide, a "first binding material" in the terminology of Durst, is carried on an absorbent material, which the examiner insists is a "sensing interface" within the meaning of the present claims. Applicants disagree. The absorbent material of Durst is not a sensing interface.

In arguing that the absorbent material of Durst is a sensing interface, the examiner makes much of the fact that an interface is a surface that forms a boundary of two, for example, phases. However, examiner focus on the term "interface" is misplaced. In the present claims the capturing oligonucleotide is bound to the "sensing interface" (emphasis added). The examiner has improperly ignored the sensing limitation in the phrase "sensing interface". The absorbent material of Durst cannot be viewed as a sensing surface. The absorbent material does no sensing. Instead, the absorbent material is merely a support for the first binding material. In Durst it is the electrodes, which Durst explains, can be above or below the absorbent material, that performs a sensing function. It is the electrodes and not the absorbent material that receive the signal that indicates whether the analyte is present or not. Thus, Durst does not disclose a device in which an oligonucleotide is bound to a sensing interface. Accordingly, Durst cannot anticipate any of claims 23-26, 28, 29 and 31.

In addition, Applicants have amended claim 23 to specify that the presence of the signal-amplifying agent on the sensing interface is detected by "monitoring electron transfer resistance of the sensing interface". Even if the absorbent material of Durst could be considered a sensing interface, which it cannot, there is nothing in Durst that suggests monitoring the electron transfer resistance of the absorbent material. For this independent reason, Durst cannot anticipate any of claims 23-26, 28, 29 and 31.

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In view of the forgoing, applicants respectfully request that the rejections under 35 U.S.C. §102(e) based on Durst be withdrawn.

Rejections Under 35 U.S.C. §103

The examiner rejected claim 3 as obvious in view of Blackburn taken with Lizardi et al. (U.S. Patent 6,143,495). According to the examiner, it would have been obvious to modify the method of Blackburn to use probes of the size described by Lizardi et al. Claim 3 depends from claim 1. As noted above, Blackburn does not disclose a method that includes "measuring insulation of the sensing interface to interfacial electron transfer between the sensing interface and the surrounding medium" as required by claims 1 and 3. Lizardi et al. does not suggest such a method. Thus, Blackburn and Lizardi et al., no matter how combined, cannot render claim 3 obvious.

The examiner rejected claim 27 as obvious in view of Durst taken with Okahata et al. According to the examiner, it would have been obvious to modify the method of Durst using the quartz crystal microbalance analysis method of Okahata et al. Claim 27 depends from claim 23. As discussed above, Durst does not describe a method in which an oligonucleotide is bound to a sensing interface as required by claims 23 and 27. Okahata et al. does not suggest such a method. Thus, Durst and Okahata et al., no matter how combined, cannot render claim 27 obvious.

The examiner rejected claim 30 as obvious in view of Durst taken with Pease et al. and Lanza et al. According to the examiner, it would have been obvious to modify the method of Durst using the biotin-based amplification method of the secondary references. Claim 30 depends from claim 23. As discussed above, Durst does not describe a method in which an oligonucleotide is bound to a sensing interface as required by claims 23 and 30. The secondary references do not suggest such a method. Thus, the cited references, no matter how combined, cannot render claim 30 obvious.

In view of the forgoing, applicants respectfully request that the rejections under 35 U.S.C. §103 be withdrawn

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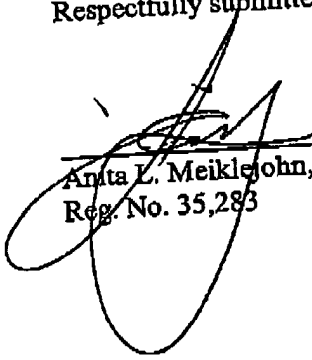
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Conclusion

Is it believed that the claims are in condition for allowance. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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Anita L. Meiklejohn, Ph.D.
Reg. No. 35,283

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-2804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

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